IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: ZAGURY3A

In re Application of:	)	Art Unit: 1648
ZAGURY et al.	)	Examiner: J. S. Parkin
Appln. No.: 09/763,369	)	Washington, D.C.
Date Filed: May 22, 2001	)	Confirmation No. 9905
For: METHOD FOR DETERMINING PROGNOSIS OF HIV...	)	

DECLARATION UNDER 37 CFR §1.132

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window
Randolph Building, Mail Stop **Amendment**
401 Dulany Street
Alexandria, VA 22314

Sir:

I, Jean-François ZAGURY, hereby declare and state as follows:

I am a co-inventor of the above-identified application and my education and professional experience is presented in the curriculum vitae attached hereto.

The raw data, from which Tables 2 and 3 of Example 1 on pages 13 and 15 of the instant specification were generated, are attached hereto as Tables A and B, respectively. I can attest of my own personal knowledge that all the raw data reported herein are true and accurate.

As can be directly determined from Table A, 45 (approximately 57.7%) out of the 78 NP-NP patients have high anti-tat antibody levels (0.31 and above, as defined in Table 2 of the above-

identified application), i.e., patients #6, 7, 9, 10, 12, 14, 16, 49, 69, 93, 114, 116, 135, 144, 147, 148, 153, 163, 169, 182, 194, 195, 209, 214, 222, 223, 224, 230, 249, 504-507, 509, 521, 527-529, 532, 539, 542, 544, 555, 558, and 577. These numbers from the raw data exactly match those presented in Table 2 of the above-identified application (i.e., 45 NP-NP patients have high anti-tat antibody levels and 33 with low anti-tat antibody levels), as would be expected since Table A presents the raw data used for Table 2 of the above-identified application. Similarly, it can be directly determined from Table A that 44 (approximately 56.4%) out of the 78 NP-NP patients have low p24 Ag levels (between 0 and 19, as defined in Table 2 of the above-identified application), i.e., patients #6, 7, 9, 10, 12, 14, 16, 49, 69, 93, 114, 116, 135, 144, 147, 148, 153, 163, 169, 182, 195, 209, 214, 222, 224, 230, 231, 249, 504-507, 509, 521, 527-529, 532, 539, 542, 544, 555, 558, and 577. These numbers from the raw data also exactly match those presented in Table 2 of the above-identified application (i.e., 44 NP-NP patients have low p24 Ag levels and 34 with high p24 Ag levels), as expected.

Importantly, it can be directly determined from Table A that, among the 45 NP-NP subjects having high anti-tat antibody levels, 43 also exhibit low p24 Ag levels (all of them except patients #194 and 223), i.e., 95.5% having both high anti-tat antibody and low p24 Ag levels. Similarly, among the 44 NP-NP subjects having low p24 Ag levels, 43 also exhibit high anti-tat antibody levels (all of them except patient #231), i.e., 97.7% thereof.

As can be directly determined from Table B, 19 (approximately 73%) out of the 26 NP-P patients have low anti-tat antibody levels (between 0 and 0.31, as defined in Table 2 of the above-identified application), i.e., patients #5, 33, 42, 50, 56, 64, 133, 146, 166, 213, 220, 225, 232, 233, 508, 535, 540, 543, and 560. These numbers from the raw data exactly match those presented in Table 2 of the above-identified application (i.e., 19 NP-P patients have low anti-tat antibody levels and 7 have high anti-tat antibody levels). Similarly, it can be directly determined from Table B that 18 (approximately 69.2%) out of the 26 NP-P patients have high p24 Ag levels (levels of 20 and above, as defined in Table 2 of the above-identified application), i.e., patients #5, 33, 42, 50, 56, 64, 133, 146, 166, 213, 220, 225, 232, 233, 508, 535, 543, and 560. These numbers exactly match those recited in Table 2 of the above-identified application (i.e., 8 NP-P patients have low p24 Ag levels and 18 have high p24 Ag levels).

Importantly, it can be directly determined from Table B that, among the 19 NP-P subjects having low anti-tat antibody levels, 18 exhibit high p24 Ag levels (all of them except patient #540), i.e., 94.7% thereof. Similarly, among the 18 NP-P subjects having high p24 Ag levels, 18 (all of them) exhibit low anti-tat antibody levels, i.e., 100% thereof.

In conclusion, the raw data in Tables A and B attached hereto clearly confirm the high correlation between the above two anti-tat antibody and p24 antigen markers and the progression or non-progression towards AIDS, as disclosed and taught in the above-

identified application (see for instance page 14, lines 18-19, page 15, lines 1-5, and page 20, lines 20-23 of the instant specification).

The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the applicatio or any patent issued thereon.

September 20, 2005
Date

J.F. Zagury
Jean-François ZAGURY

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Codes	Anti-Tt	Anti-Tat	Anti-Nef	p24	Anti-p24	Viral Load
6	0,906	0,490	0,105	7,580	1,713	3,478
7	0,796	0,349	1,494	2,517	2,280	1,722
8	0,494	0,279	0,104	27,377	0,279	3,907
9	0,353	0,825	0,081	2,819	2,222	1,944
10	0,450	0,730	0,160	4,033	2,166	2,010
12	2,059	0,776	0,358	8,683		2,051
13	0,271	0,152	0,083	26,734	2,218	3,420
14	0,890	0,407	0,106	4,186		1,634
15	1,108	0,282	0,084	30,839	2,207	3,140
16	0,459	0,363	0,115	6,650	2,194	3,941
17	0,419	0,272	0,189	27,749	2,229	3,669
19	0,163	0,279	0,256	31,039	0,595	3,621
27	0,754	0,194	0,121	27,285	2,213	4,967
34	0,428	0,163	0,126	30,343	1,377	4,524
35	1,253	0,222	0,167	35,744	0,796	4,659
49	1,115	0,377	0,134	17,272	0,613	4,617
53	0,723	0,244	0,169	28,125	0,732	4,628
57	0,364	0,266	0,072	39,563	1,577	4,683
69	1,320	0,894	0,882	9,473	2,266	1,234
93	1,513	0,874	0,124	3,122	0,366	4,023
104	0,493	0,302	0,464	50,192	0,287	4,000
106	1,245	0,300	0,499	30,939	2,237	4,880
112	1,313	0,191	0,070	39,216	0,776	1,900
114	1,721	0,396	0,337	7,898	2,254	1,930
116	0,911	0,357	0,082	4,186	2,079	4,392
127	0,195	0,234	0,096	41,796	2,107	4,362
135	0,035	0,311	0,077	3,425	2,267	4,457
144	0,144	0,438	0,493	18,945	2,214	3,570
145	0,911	0,190	0,164	29,366	2,157	1,600
147	1,049	0,711	0,202	4,951	2,149	4,663
148	0,877	0,336	0,079	4,339	0,163	4,312
153	0,480	0,383	0,135	3,273	2,274	4,404
160	0,331	0,299	0,069	35,853	2,215	
163	0,469	0,381	0,083	11,386	0,294	3,689
169	0,154	0,708	0,146	5,721	2,237	2,012
182	0,380	0,661	0,282	3,425	0,241	3,850
190	0,385	0,296	0,167	35,093	0,290	4,480
191	0,049	0,209	0,095	32,563	0,208	4,230
193	0,812	0,235	0,077	27,937	2,210	1,220
194	1,579	0,466	0,431	19,620	1,402	1,340
195	0,211	0,321	0,117	5,105	2,148	1,450
201	0,340	0,195	0,099	45,217	0,224	4,290
206	0,568	0,137	0,090	28,693	0,156	2,760
207	0,249	0,233	0,296	31,240	0,593	1,100
209	1,165	0,643	0,691	11,226	2,242	1,440
211	0,723	0,284	0,641	43,121	0,581	1,650
214	1,163	0,344	0,193	6,650	2,172	4,340
221	0,149	0,223	2,176	27,008	2,223	2,920
222	0,175	0,317	0,133	2,970	2,226	1,890
223	1,044	0,356	0,073	51,776	2,269	4,300
224	1,348	0,328	0,105	8,369	0,802	4,320
229	0,017	0,178	0,100	28,408	2,210	2,670

230	0,710	0.561	0,494	3,729	0,983	4,030
231	0,999	0.304	0,189	4,186	1,617	4,370
249	0,311	0.405	0,116	4,339	0,184	4,160
250	0,877	0,174	0,180	35,418	2,180	4,850
504	0,655	0,369	0,147	11,066	2,111	4,550
505	1,485	0,386	0,472	4,339	1,468	3,850
506	1,088	0,371	0,078	11,226	2,094	4,430
507	1,549	0,457	0,237	8,369	0,407	4,150
509	1,106	0,572	0,223	3,729	2,175	4,190
514	0,678	0,289	0,064	34,025	2,211	1,600
521	0,416	0,402	0,144	4,644	2,102	4,030
527	1,822	0,326	0,233	3,577	2,223	1,000
528	1,707	0,401	0,105	3,577	1,838	1,000
529	0,797	0,319	0,273	9,632	1,713	2,680
531	0,595	0,278	0,503	39,794	2,204	1,100
532	0,543	0,368	0,503	14,793	2,206	2,200
539	1,396	0,481	0,054	4,951	1,083	1,000
541	1,023	0,179	0,094	44,471	0,256	3,440
542	1,635	0,527	0,298	5,258	2,214	1,900
544	1,179	0,336	0,076	5,412	2,303	1,250
551	0,232	0,271	0,311	37,962	1,931	3,550
555	1,416	0,390	0,186	16,110	2,227	2,890
558	0,584	0,416	0,158	4,033	0,693	4,740
559	0,467	0,177	0,220	28,693	1,846	4,150
576	0,810	0,251	0,070	38,075	0,320	5,000
577	0,278	0.370	0,407	4,951	2,202	5,000

Codes	Anti-Tt	Anti-Tat	Anti-Nef	p24	Anti-p24	Viral Load
5	0,314	0,220	0,345	27,192	2,203	3,712
33	0,815	0,222	0,131	30,442	2,049	1,890
42	0,101	0,182	0,060	31,846	2,115	4,660
50	0,853	0,229	0,094	39,563	0,339	3,310
56	0,855	0,235	0,076	28,030	1,889	3,871
64	0,955	0,220	0,067	37,962	0,367	4,443
76	0,827	0,332	0,110	4,033	2,252	5,000
133	0,574	0,229	0,273	31,948	0,592	4,703
137	1,275	0,423	0,143	4,186	2,200	4,200
146	0,594	0,287	0,284	37,850	1,482	4,361
166	0,106	0,209	0,087	38,987	2,221	4,990
168	0,625	0,369	0,294	4,644	2,192	4,461
212	1,168	0,330	0,123	3,425	2,190	4,040
213	0,091	0,238	0,105	32,666	0,800	3,100
220	0,523	0,180	0,069	39,794	1,162	4,050
225	0,414	0,202	0,058	40,729	1,505	1,110
232	0,694	0,266	0,134	38,643	2,163	2,580
233	0,389	0,189	0,125	42,758	1,259	4,020
238	0,988	0,626	0,241	11,386	0,317	4,320
508	0,317	0,202	0,147	40,494	2,201	4,490
533	0,974	0,676	0,864	3,729	2,148	3,820
535	0,243	0,296	0,089	42,155	2,204	4,430
540	1,513	0,303	0,167	4,186	2,239	3,790
543	0,920	0,226	0,092	32,357	2,236	2,580
560	0,830	0,170	0,389	36,511	0,500	4,090
578	0,769	0,480	0,233	5,105	2,073	5,000

Curriculum Vitae

- *Civil status*

Single

- *Degrees and diplomas*

1982 : Ecole Normale Supérieure rue d'Ulm (Section Maths), Paris

1985 : Master's degree in Immunology, Institut Pasteur, Paris
Master's degree in Artificial Intelligence, Ecole des Ponts et Chaussées, Paris

1991 : PhD in Immunovirology, University Paris VI, Paris

1992 : Medical Degree, Faculté Broussais/Hotel-Dieu, Paris

1994 : Habilitation à Diriger des Recherches, University Paris VI, Paris

1996 : Associate Professor at the Institute of Human Virology
University of Maryland, Baltimore, USA

2000 : Associate Professor at Temple University, Philadelphia, USA

2003 : Professor, Chair of the Department of Bioinformatics at Conservatoire National des Arts et Métiers, Paris.

- *Professional experience*

1987-1988 : Researcher at the Laboratory of Tumor Cell Biology, NIH, Bethesda, USA (Pr RC. Gallo)
1991 to 1995 : Post-Doc in the Laboratoire de Physiologie Cellulaire, University Paris VI, Paris (Pr D. Zagury)
1996 : Associate Professor at the Institute of Human Virology, Baltimore, USA (Pr Gallo)
1997 to 1999 : Senior Scientist at the Laboratoire de Physiologie Cellulaire, University Paris VI, Paris (Pr D. Zagury)
1999 to 2001 : Associate Professor at the Department of Neurovirology and Cancer, Temple University, Philadelphia (Pr K. Khalili)
2002-2003 : Scientific Director of the company Neovacs SA, Paris, France

- *Current position*

Chair of the department of Bioinformatics at Conservatoire National des Arts et Métiers, Paris University, France.

- ***University teaching responsibilities (academic year), level (undergraduate, masters, postgraduate, continuing training, ...), university, town/city, duration (hours of teaching per year) and exact title of position***

1993-2003 : Co-supervisor of the Master's degree "DEA de Biologie Cellulaire et Moléculaire", University Paris VI, Paris.
Organizer and coordinator of a full week course (30 hours) on :
"Les réseaux moléculaires de communication cellulaire et matricielle. Leur rôle dans les grandes fonctions physiologiques"

Supervisor (Directeur de thèse) of former PhD students :
1998 : Y-Y. Cho, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse
1998 : R. Ivanova, Thèse de Doctorat de l'Université de Paris VII, Directeur de thèse
1999 : H. Hendel, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse
On-going PhDs :
2003 : E. Regulier, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (3rd year)
2003 : C. Capini, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (3rd year)
2003 : S. Bertin, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (2nd year)
2003 : A. Vasilescu, Thèse de Doctorat de l'Université d'Orsay, Directeur de thèse, (2nd year)
2003 : H. Do, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (1st year)

Supervisor of Masters' interns (6 to 8 months-long internships):
2000 : E. Regulier, Master's degree in Biotechnology (ESIL, Marseille), Directeur de stage
2000 : C. Capini, Master's degree in Biotechnology (ESIL, Marseille), Directeur de stage
2001 : S. Bertin, Master's degree in Biotechnology (ESIL, Marseille), Directeur de stage
2001 : A. Vasiles, Master's degree in Genomics (Université d'Orsay), Directeur de stage
2001 : S. Tamim, Master's degree in Bioinformatics (DESS, ISTIA, Angers), Directeur de stage
2001 : A. Maze, Master's degree in Bioinformatics (DESS, Université d'Évry), Directeur de stag
2002 : H. Do, Master's degree in Cell and Molecular Biology (DEA, Paris VI), Directeur de stage
2002 : G. Diop, Master's degree in Cell &Molecular Biology (DESS, Nancy I), Directeur de stage
2002 : FX. Goutailler, Master's degree in Bioinformatics (DESS, Paris VII), Directeur de stage
2002 : L. Autin, Master's in Bioinformatics (DEA, Paris VI), co-Directeur de stage
2002 : O. Agopian, Master's degree in Bioinformatics (École Polytechnique), Directeur de stage
2002 : L. Jacquemin, Master's degree in Statistics, (ENSAE Bretagne), co-Directeur de stage
2003 : T. Hirtzig, Master's degree in Genomics (DEA, Université d'Orsay), Directeur de stage
2003 : E. Muel, Master's degree in Cell &Molecular Biology (DESS, Nancy I), Directeur de stag
2003 : E. Bernier, Master's degree in Biotechnology (DU, Paris VI), Directeur de stage
2003 : M. Laborie, Master's degree in Biotechnology (DU, Paris VI), Directeur de stage
2003 : H. Kanas, Master's degree in Bioinformatics (DEA, Université d'Evry), Directeur de stag
2003 : A. Benais, Master's degree in Bioinformatics (DESS, Paris VI), Directeur de stage
2003 : S. Chiusa, Master's degree in Bioinformatics (DESS, Toulouse), Directeur de stage

- ***Membership of learned societies, discussion groups (organization concerned and period of duty)***

Member of the American Association for the Advancement of Science (AAAS) since 1989
Member of the American Association for Microbiology (ASM) since 1989

SUMMARY OF THE WORK

PHARMACOGENOMICS OF AIDS, DEVELOPMENT OF NEW BIOINFORMATICS AND NEW THERAPEUTIC PLATFORMS.

" # " refers to the publication number in my list of publications

Past work : During my PhD, I have sequenced the HIV-2NIHZ viral isolate and confirmed that HIV-2 was as diversified as HIV-1 (JF Zagury et al, PNAS, 1988 #8). During my Post-Doc, I focussed on the mechanisms of immunopathogenesis of HIV-1. I identified viral sequences possibly interfering with the immune system. For this, I developed an original software, AUTOMAT, able to identify systematically all similarities between a given sequence and that in a data bank. AUTOMAT was programmed in 1991-1993 and published in 1994 (H. Cantalloube et al. Bioinformatics, 1994 #23; ibid, 1995 #31). AUTOMAT is as powerful as BLAST for protein comparisons and even more efficient for DNA comparisons. Thanks to AUTOMAT, we identified striking similarities between HIV-1 and CD4 and Fas molecules. Analysis of the immune response in presence of peptides suggested a possible role of these similarities in immune dysregulation (JF Zagury et al, PNAS, 1993 #20).

In 1995, I tried to investigate AIDS disease mechanisms through a genomic approach. For this, I set-up the GRIV (Genetics of Resistance/suceptibility to Immunodeficiency Virus) cohort, of extreme patients, slow (SP) and rapid progressors (RP). GRIV is now the largest cohort of its type in the world with 300 SP and 100 RP patients. The SP patients correspond to 1% of the infected patients, so that the cohort is equivalent to the extent of 30 000 patients at all stage of disease.

We have initially shown that SP patients who remained stable during 2 years follow-up were those exhibiting Abs against the Tat protein in their serum, and that Tat Abs were inversely correlated to p24 antigenemia. This has been the rationale for the development of a vaccine targeting the Tat protein (JF Zagury et al, J Hum Virol. 1998 #41; A Gringeri et al, ibid, 1998 #42; A Gringeri et al, JAIDS 1999 #47). A Phase II clinical trial lead by a Major Pharma is ongoing on that candidate vaccine.

GRIV is mainly a pharmacogenomic project designed to understand the pathogenetic mechanisms of HIV-1 by analyzing gene associations. We confirmed the CCR5- 32, CCR2-64I associations (Rappaport et al, Lancet 1997 #37, Hendel et al, J AIDS Acquired Immunodef Synd 1998 #43) and discovered new HLA associations (Hendel et al, J Immunol 1999 #48; Flores-Villanueva et al, J Immunol, in press. #64). Since 2001, the project has taken a new dimension thanks to the collaboration with the National Center for Genotyping (CNG, Evry). High throughput genotyping has allowed to focus on cytokines as candidate genes. We have identified major associations, especially in key Th1/Th2 cytokines such as IL4, IL10 (Vasilescu et al. Genes Immunity, in press. #65). Three major associations have not yet been published because they appear to be as important as the CCR5- 32 mutation and we wish to investigate them more throroughly to understand the underlying biological explanation.

On-going Directions : The GRIV pharmacogenomic project, thanks to the critical size of the cohort, is now yielding important information. We plan to finish in priority the cytokine receptor genes. A genome-wide approach is under consideration because of the power of the cohort. The software already conceived, SCAGEN still needs to integrate haplotype treatment and compute genetic distance between populations. SCAGEN is a bioinformatics platform which should prove useful for all pharmacogenomics projects.

My second major project is to develop a new therapeutic platform : active immunization against cytokines. The high potential of this new therapeutic strategy has been proven for various diseases in mice models (IL9, IL5, TNF) but also in humans (IFN . .). It could apply in autoimmune diseases, certain cancers and allergy. My strategy is to target peptides derived from the cytokine domain binding to the receptor. A patent has been taken on that new approach. The 3-D structure of cytokines is well-known, making it easy to design peptides harboring a conformation similar to that in the native cytokine. I have started a collaborative work with the group of JP Mornon (Univ Paris VI) and S. Muller (CNRS, Strasbourg) to rationally design and produce such peptides susceptible to generate neutralizing Abs. Murine models for Rheumatoid Arthritis, for Multiple Sclerosis and for Autoimmune Diabetis are to be tested in collaboration with experts in the field (MC Boissier, Hôp Bobigny, R Liblau, Hôp Salpétrière, C. Boitard, Hôp St-Vincent de Paul).

I. PUBLICATIONS

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2. Franchini G., E. Collalti, S.K. Arya, E.M. Fenyo, G. Biberfeld, **J-F. Zagury**, P.J. Kanki, F. Wong-Staal, R.C. Gallo. Genetic analysis of a new subgroup of human and simian T-lymphotropic retroviruses : HTLV-IV, LAV-2, SBL-6669, and STLV-III$_{agm}$. *AIDS Res Human Retroviruses* (1987) 3, 11-17.

3. Arya S.K., B. Beaver, L. Jagodzinski, B. Ensoli, P.J. Kanki, J.Albert, E.M. Fenyo, G. Biberfeld, **J-F. Zagury**, F. Laure, M. Essex, E. Norrby, F. Wong-Staal, R.C. Gallo. New human and simian HIV-related posess functional transactivator (tat) gene. *Nature* (1987) 328, 548-550.

4. Leonard R., D. Zagury, I. Desportes, J. Bernard, **J-F Zagury**, R.C. Gallo. Cytopathic effect of HIV in T4 cells is linked to the last stage of virus infection. *Proc Natl Acad Sci USA* (1988) 85, 3570-3574.

5. **Zagury J-F.**, G. Franchini, M. Reitz, E. Collalti, B. Starcich, L. Hall, K. Fargnoli, L. Jagodzinski, F. Laure, S.K. Arya, S. Josephs, D. Zagury, F. Wong-Staal, R.C. Gallo. Genetic variability between isolates of human immunodeficiency virus (HIV) type 2 is comparable to the variability among HIV type 1. *Proc Natl Acad Sci USA* (1988) 85, 5941-5945.

6. Agius G., V. Vaillant, G. Dindinaud, M. Bazillou, J-F. **Zagury**, V. Kolenitchenko, M. Castets. HTLV-1, HIV-1 and HIV-2 seroprevalences in Guadeloupe, French West Indies. *Eur J Epidemiol* (1989) 5, 532.

7. Mars M., J-F. **Zagury**, I. Fossati, G. Beaud. Variable proteolytic cleavage of gag precursor expressed after infection of several cell lines with an HIV-2 gag-pol recombinant vaccinia virus. *AIDS Res Hum Retroviruses* (1990) 6, 271-273.

8. **Zagury J-F.**, S.F. Josephs, G. Agius, I. Nicol, A. Willer, V.S. Kalyanaraman, D. Zagury, F. Wong-Staal, R.C. Gallo. In vitro characterization of a biologically active molecular clone of HIV-2 (NIHZ) containing a nef deletion and expressing a full-length transmembrane protein. *AIDS Res Human Retroviruses* (1990) 6,1079-1085.

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10. Callebaut I., J-F. **Zagury**, D. Portetelle, A. Burny, D. Zagury. Sequence homologies between HIV envelope and alpha1 antitrypsin suggest a new way to understand the cleavage mechanism and infectivity. *Archives Internationales de Physiologie, de Biochimie et de Biophysique.* (1991) 99, B50.

11. Zagury D., Bernard J., Halbreich A., Bizzini B., Carelli C., Achour A., Defer M.C., Bertho J.M., **Zagury J-F.**, Salaun J.J., Lurhuma Z., Aboud-Pirak E., Lowell G., Lebon P., Burny A., Picard O. One-Year follow-up of vaccine therapy in HIV-infected immune deficient individuals: A new strategy. *J Acquir Immune Defic Syndr* (1992) 5, 676-681.

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II. TECHNOLOGY TRANSFER

1. WO 92/22577 du 17/6/1991.
Active immunization against cytokines. Issued in Europe, USA and Canada. **Licensed.**

2. WO 94/03487 du 10/8/1993.
Immunosuppressive HIV-1 peptides. Issued en Europe

3. WO 96/27389 du 8/3/1995.
Immunisation against retroviral proteins. Issued in Europe, USA and Canada
Licensed

4. PCT/FR98/02727 du 14/12/1997
New immunogens anti-HIV1 (toxoids), methods of preparation and application to the prevention and treatment of AIDS. Under PCT
Licensed

5. PCT/US99/18770 du 21/8/1998
Methods for determining the disease prognosis following HIV-1 infection or immunisation against Tat. Under PCT

6. WO 00/03732 du 15/6/1999
Immunisation against proteins with local action. Under PCT.

7. WO 00/64937 du 26/4/1999
New immunogens derived from inactivated cytokines. Under PCT.

8. WO 01/43771 du 15/12/1999
Mucosal immunity against immunosuppressive proteins. Under PCT.

9. FR 0010480 du 9/8/2000
Immunisation against factors from tumor microenvironment. Under PCT.

10. Patent de 12/2001.
Mutated Tat protein.

12. FR0204464 du 10/4/2002.
Peptidic epitopes from cytokines.

13. Software **AUTOMAT** (1993). Copyright JF Zagury.

14. Software **SCAGEN** (2001). Copyright JF Zagury.

III. DIRECTING RESEARCH

On-going PhD students :

E. Regulier, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (3rd year)
C. Capini, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (3rd year)
S. Bertin, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (2nd year)
A. Vasilescu, Thèse de Doctorat de l'Université d'Orsay, Directeur de thèse, (2nd year)
M. Foglio, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (2nd year)
H. Do. Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse, (1st year)

On-going Master's degree students :

T. Hirtzig, Master's degree in Genomics (DEA, Université d'Orsay), Directeur de stage
E. Muel, Master's degree in Cell &Molecular Biology (DESS, Nancy I), Directeur de stage
E. Bernier, Master's degree in Biotechnology (DU, Paris VI), Directeur de stage
M. Laborie, Master's degree in Biotechnology (DU, Paris VI), Directeur de stage
H. Kanas, Master's degree in Bioinformatics (DEA, Université d'Evry), Directeur de stage
A. Benais, Master's degree in Bioinformatics (DESS, Paris VI), Directeur de stage
S. Chiusa, Master's degree in Bioinformatics (DESS, Toulouse), Directeur de stage

Director of the former PhD students:

1998 : Y-Y. Cho, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse
1998 : R. Ivanova, Thèse de Doctorat de l'Université de Paris VII, Directeur de thèse
1999 : H. Hendel, Thèse de Doctorat de l'Université de Paris VI, Directeur de thèse

Supervisor of the former Masters' interns (6 to 8 months-long internships):

2000 : E. Regulier, Master's degree in Biotechnology (ESIL, Marseille), Directeur de stage
2000 : C. Capini, Master's degree in Biotechnology (ESIL, Marseille), Directeur de stage
2001 : S. Bertin, Master's degree in Biotechnology (ESIL, Marseille), Directeur de stage

2001 : A. Vasiles, Master's degree in Genomics (Université d'Orsay), Directeur de stage
2001 : S. Tamim, Master's degree in Bioinformatics (DESS, ISTIA, Angers), Directeur de stage
2001 : A. Maze, Master's degree in Bioinformatics (DESS, Université d'Évry), Directeur de stage
2002 : H. Do, Master's degree in Cell and Molecular Biology (DEA, Paris VI), Directeur de stage
2002 : G. Diop, Master's degree in Cell &Molecular Biology (DESS, Nancy I), Directeur de stage
2002 : FX. Goutailler, Master's degree in Bioinformatics (DESS, Paris VII), Directeur de stage
2002 : L. Autin, Master's in Bioinformatics (DEA, Paris VI), co-Directeur de stage
2002 : O. Agopian, Master's degree in Bioinformatics (École Polytechnique), Directeur de stage
2002 : L. Jacquemin, Master's degree in Statistics, (ENSAE Bretagne), co-Directeur de stage

SCIENTIFIC COLLABORATIONS

The GRIV project involves the following groups:

GRIV PROJECT COLLABORATIONS

Dr Mark Lathrop, Centre National de Génotypage, Evry, France
Collaboration on genotyping

Dr Catherine Huber, Unité Biotatistique, Université Paris V, France
Collaboration on Statistics

Dr Pedro Flores-Villanueva, Harvard Medical School, Boston
Collaboration on genotyping

Dr Steve O'Brien Laboratory of Genomic Diversitry, National Cancer Institute, Frederick
Collaboration on genotyping

Dr Jay Rappaport, Temple University, Philadelphia
Collaboration on promoter activity of various cytokine genes

The project on active immunization against cytokines involves the following groups :

COLLABORATIONS ON ACTIVE IMMUNIZATION AGAINST CYTOKINE PEPTIDES

Dr Jacques Chomilier, Laboratoire de Minéralo-Cristallographie, Université Paris VI
Collaboration on molecular modelling

Dr Sylviane Müller, Laboratoire d'Immunologie, CNRS, Strasbourg
Collaboration on design of cytokine peptides and animal models

Dr Christian Boitard, Hôpital St-Vincent de Paul
Collaboration on murine type I diabetis models

Dr Roland Liblau, Hôpital La Salpétrière
Collaboration on murine Multiple Sclerosis models

Dr Marie-Christophe Boissier, Hôpital Bobigny
Collaboration on murine Rheumatoid Arthritis models